REMARKS/ARGUMENTS

Claims 1, 2, 5-14, 16 and 17 are pending. Claims 1 and 11 are amended. Claims 3, 4 and 15 were previously cancelled. Applicant reserves the right to present any withdrawn or canceled subject matter in one or more continuation or divisional applications.

Rejections under 35 U.S.C. § 103

Claims 1-2, 5-14, and 16-17 have been rejected under 35 U.S.C. §103(a) as being unpatentable over PCT WO 92/13549 to Hathaway et al.

It is submitted that the pending claims are not obvious in view of Hathaway et al. Hathaway et al. fails to disclose the specific tripeptide derivatives of present formula (I). Further, Hathaway et al. fails to disclose the treatment of the diseases recited in claim 1. There is no suggestion in Hathaway to treat neurodegenerative diseases by administering a compound of formula I as recited in independent claim 1.

The Examiner's attention is drawn to the claims as presently presented. Hathaway et al. does not describe tripeptide derivatives which are amidated, i.e., have a substituent as defined in present formula (I), where X is NH_2, NH-C_{1-3}-alkyl or N(C_{1-3} alkyl)$_2$. There would have been no motivation for the skilled person to amidate a proline residue. Moreover, the amidation described in the application results in advantageous properties which makes them useful for the treatment of neurodegenerative diseases. There would have been no motivation from the disclosure of Hathaway et al. to make the amidated tripeptide derivatives recited in the claims, or to use them for treatment as claimed.

The amidation results in an increased affinity constant to the tyrosine kinase C receptor (TrkC), as shown in the table on page 23 of the present application (compare Gly-Phe-ProNH_2 with Gly-Phe-Pro-OH). Further, the amidation results in an improved passage of the brain blood barrier (see again the table on page 23 of the present application).

These improvements due to the amidation were surprising and unexpected. Hathaway et al. provides no motivation for the skilled person to amidate the proline residue to improve the affinity to TrKC or the passage of the brain blood barrier. Nothing in Hathaway et al. suggests the compounds recited in the claims or their unexpected properties.

Hathaway et al. describes the inhibition of cell preliferation of smooth muscle cells with certain peptides. This effect is deemed useful for the prevention of arterial occlusion and the prevention and treatment of arteriosclerosis (see for example, page 1, lines 21 to 30). In contrast, the present claims are directed to the treatment of neurodegenerative diseases, i.e. the substances act on nerve cells. From the teachings of Hathaway et al., there would have been no suggestion of the claimed methods.

The Examiner has noted some studies involving patients having arteriosclerosis and a neurodegenerative disease such as Alzheimer's disease, and speculates that the diseases are interrelated. However, there does not appear to be any support for Examiner's conclusion that "treating arteriosclerosis would have an intrinsic effect upon Alzheimer's disease." These diseases are distinct, and one skilled in the art, such as a physician prescribing therapy, would not expect that compounds effective in one of the diseases would necessarily be effective in the other.

The methods of treating neurodegenerative diseases using the amidated tripeptides recited in the claims would not have been obvious to one of skill in the art in view of Hathaway et al. Nothing in the other references cited by the Examiner provides any additional disclosure that would have rendered the specifically claimed methods obvious. Withdrawal of this rejection is therefore respectfully requested.

Obviousness-Type Double Patenting Rejections

Claims 1-2, 5-10, and 16 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-2 and 5-8 of copending U.S. Patent Application No. 10/635,805.

It is submitted that these claims do not cover overlapping subject matter. A postlesional neuronal disease due to ischemia or traumatic impact, as recited in the claims of the '805 application, is not the same as a neurodegenerative disease as recited in the current application. In support of this, Alzheimer's disease and postlesional diseases due to ischemia are differently classified by the World Health Organization. Distinct classification and therapy exist for the diseases.

Withdrawal of this rejection is therefore respectfully requested.

Conclusion

In view of the above arguments, withdrawal of the outstanding rejections is respectfully requested. The Commissioner is authorized to charge any fees associated with this filing to Deposit Account 11-0980.

Respectfully submitted,

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